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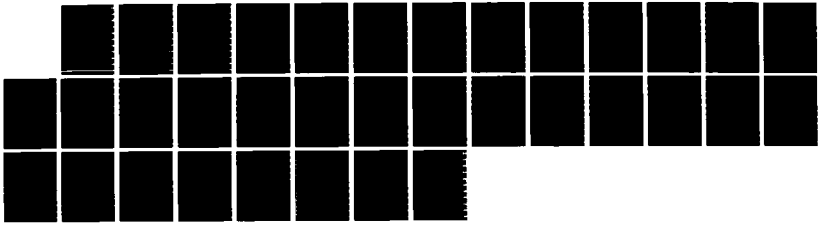

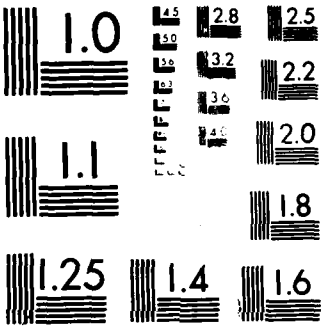

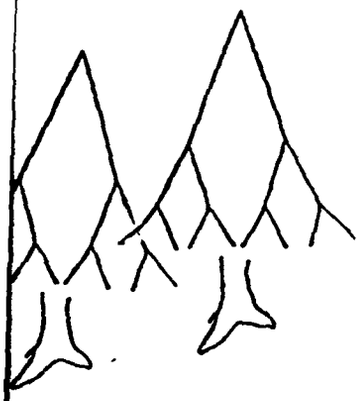

Cognitive Science Program

COMPONENTS OF THE MOTOR PROGRAM: THE CEREBELLUM AS AN INTERNAL CLOCK

RICHARD B. IVRY AND STEVEN W. KEELE

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This report summarizes the initial phase of our research with neurological patients on timing functions. Parkinsonian, cerebellar, cortical and peripheral neuropathy patients as well as college aged and elderly control subjects were tested on two separate measures of timing functions. The first task involved the production of timed intervals and used the repetitive tapping task developed by Wing and Kristofferson (1973). The second task measured the subjects' perceptual ability to discriminate comparable temporal intervals. The tapping results indicate that cortical, cerebellar, and peripheral neuropathy patients are more variable in

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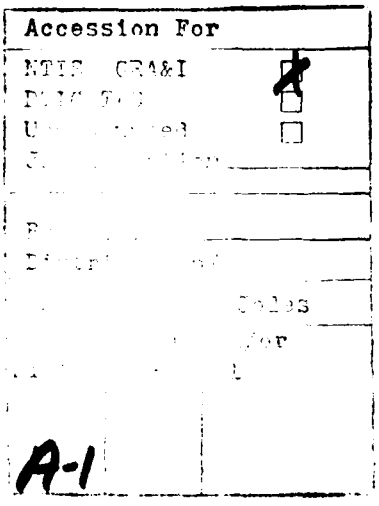
implementing their responses. In addition, the cortical and cerebellar patients demonstrate increased variability in an internal timekeeping process. A small number of basal ganglia (Parkinson) patients also showed a deficit in the timing process. These results are accounted for by postulating that the timing of interval can only commence once the central command for the preceding response has been issued. Thus, deficits in any central neural system can affect the integrity of the timing process. Nonetheless, the cerebellum appears to play a primary role in timing functions since the cerebellar patients were the only group who showed a deficit in the perception of time task.



Components of the motor program: The cerebellum as an internal clock.

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The concept of the motor program has proved useful to researchers attempting to explain how voluntary movements are controlled. As developed by Henry and Rogers (1960) and extended by Keele (1968) among others, the motor program is an abstract representation of an intended movement, containing not only the goal of the action and the existing environmental conditions, but also the possible means by which the movement could be achieved. The motor program is analagous to the role of software used by computers: Flexible as a function of the input, but constrained within the limitations of the hardware. The program is the most general description of the capabilities of the system.

A logical extension of the computer metaphor is to consider what may be the internal procedures which form the motor program. As a starting point in our effort to develop a computational model of motor control, we have tried to hypothesize what may be the basic procedures contained in the motor program. For instance, some of the computations that may be required could involve procedures to control the selection of muscles, the sequencing of the selected muscles, and the specification of the the force and time parameters for each of the selected muscles. (see Figure 1) Thus, to throw a baseball, the system must select which arm to use, sequence the many muscles which are involved in the act of throwing (as well as make the necessary postural adjustments via other muscles), and set the activation levels for each muscle. A fastball and an off-speed pitch may involve identical temporal patterns with the only difference being that the force output is increased for the fastball. On the other hand, throwing a curveball may require an additional movement segment in which the wrist is snapped at a particular point in time.

We recognize that these hypothesized procedures may not be the actual ones embodied in the nervous system (e.g. Stein, 1982; Feldman, 1986). For example, higher order variables such as velocity may be the actual computational product rather than the consequence of the interaction of force and timing factors. Certainly the simple model outlined in the preceeding paragraph requires a very complicated control mechanism which keeps track of the various computations. Nonetheless, it is still possible that even in a more heterarchical model of motor control, some of these computations may be explicitly determined.

We have employed a three-pronged research strategy in our effort to determine the validity of these procedures. Our initial efforts using the correlational approach has been the subject of previous publications (Keele, Pokorny, Corcos, and Ivry, 1985a; Keele, Ivry, and Pokorny, submitted). In these studies we have tested the notion that there may be general (and independent) procedures for force and timing. If there exist mechanisms which are responsible at an abstract level for the computation of either force or timing, then we should find correlations across tasks which make use of common procedures under divergent experimental conditions. We have found this prediction to be borne out. For instance, subjects who are good at maintaining an arbitrary rhythm with one effector such as the hand are also good at the same task when using a

different effector such as the foot (Keele et al, 1985a). More suprising, there is a correlation between subjects' ability in timing production tasks and tests of timing perception when the durations of time are comparable across the two domains. We take these results as providing strong evidence for a common timeKeeping mechanism which is used in both production and perception functions which involve time-related decisions.

We have found similar, high correlations in motor production tasks which examine subjects' ability to control their force output (Keele et al, submitted). Importantly, we have found that these results can not easily be accounted for by postulating some general factor which supercedes these more, specific factors. If this were the case, we would expect to find high correlations across tests of timing and force or between either of these factors and a third, independent factor. We have not found this to be the case.

A second paradigm which has been used in our laboratory to study the procedures of the motor program rests on the dual-task methodology. The logic of this approach is that one should observe more interference between two tasks which share a common procedure than between tasks which can be performed independently. The results of one extensive study using this approach are reported in Pokorny (1985). While not contradictory to the correlational findings, the interpretation of these experiments only indirectly support the notion of a common mechanism which may be used in both the production and perception of time.

A third way in which we have been investigating the validity of these hypothesized procedures is by testing patients in an attempt to demonstrate that certain neurological deficits are associated with difficulty in specific tasks. We believe that our correlational work has yielded model tasks which can assess the functioning of separable components of the motor program such as force control or timing. Different patient groups can then be tested on these same tasks in an effort to show dissociations between the patients as a function of the location of their neurological lesion. To give a hypothetical example, suppose that we found that patients who had damage in the supplementary motor area had difficulty in our force control task whereas Parkinson patients, cerebellar patients, or patients with lesions in the primary motor cortex did not. This would then imply that the supplementary motor area plays a primary role in the regulation of force output, or at least is part of a force control pathway.

In this report, we will discuss our preliminary results using the neurological approach on the timing procedure. We have tested a number of different populations on our timing tasks including both college-aged and elderly control groups and patients with either cortical or subcortical lesions.

Previous research in our laboratory (Wing, Keele, and Margolin, 1984) had revealed a deficit in timing functions, at least in our production task, in a patient with unilateral symptoms of Parkinson's Disease. The primary neurological damage in Parkinson's Disease is presumed to be in the dopamine pathways of the basal ganglia. However, in another single subject study (Keele, Manchester, and Rafal, 1985b), a patient with unilateral damage to the cerebellum was also found to have a difficulty in producing regular timed intervals. Taken together, the two case studies would appear to implicate both subcortical structures in timing functions and thus bolster the argument that timing may involve some sort of pathway which passes through both regions. The perception of time task may be one way in which we could test whether either region plays a

primary role in timing. However, unlike the motor systems which are generally lateralized, the auditory input pathways project to both the contra- and ipsi-lateral side, at least at the cortical level (Moyer, 1980). Little work has been done on auditory projections to the basal ganglia and cerebellum (but see Yeo, Hardiman, and Glickstein, 1985b). Given these facts, the perception task does not easily lend itself to the single subject methodology.

It should also be noted that we have found results which contradict those cited above. For example, many Parkinson patients show no deficit in the timing task. These divergent results could be accounted for by the fact that Parkinson's Disease is not a single pathology characterized by common symptomology, but rather can be manifested in a variety of ways. The various forms may be the result of differential damage within the basal ganglia or different organization of the basal ganglia across patients.

The wide range of results we had found in our initial neuropsychological experiments led to a change in strategy in which we decided to employ a group study design in addition to the single subject studies. The relative merits of each approach have been extensively debated in the neuropsychological literature (e.g. Kertesz, 1983). Case study reports can be extremely informative since the same subject provides both the control and experimental data. However, this approach may lead the researcher to emphasize the exception rather than the rule. Group studies, by definition, avoid this potential pitfall. However, they can be quite difficult with human neurological populations since the lesion will vary greatly from subject to subject. This would tend to obscure any common deficits which may exist across the patients. The best way to overcome this problem, of course, is to have a sufficiently large number of subjects in each group, thus increasing the probability that any differences between the groups will emerge.

It has not been difficult for us to locate Parkinson patients for our studies, either through neurology clinics or patient support groups. However, cerebellar patients have proved to be much more elusive. Our desire to conduct group neuropsychological research with cerebellar patients was made possible by our association with Dr. Christopher Diener of Tuebingen University in West Germany. Dr. Diener is a neurologist at the medical school in Tuebingen and, in conjunction with Dr. Johannes Dichgans, has established an outstanding clinical and research laboratory specializing in cerebellar disorders. Dr. Diener invited us to visit his laboratory and test a number of his cerebellar patients on our motor and perceptual tasks. In addition, he provided us with access to other patients who were at the clinic.

There are a number of converging lines of evidence which have led researchers to suspect that some of the functions of the cerebellum involve timing control. One of the first theoreticians to explicitly implicate the cerebellum in timing functions was Braitenberg who published an article in 1961 titled, "Is the cerebellar cortex a biological clock in the millisecond range?" as the intuitive culmination of his anatomical observations (see also Braitenberg and Onesto, 1962; Braitenberg, 1965). Braitenberg was struck by the unusual histological invariance of the cerebellum such as the absence of folds across the folia and the flat dendritic trees of the Purkinje cells. This invariance led him to suspect that the cerebellar cortex performs some simple, unitary operation. Using this assumption as a starting point, he then noted that a single parallel fiber will make contact with hundreds of Purkinje cells, but with only a single synapse per Purkinje due to the orthogonal arrangement between the parallel fibers and the Purkinje cells. Braitenberg points out that the common

source of this signal would be lost unless the system can incorporate some sort of scheme based on delay lines which vary as a function of the distance between the input and output signal. Parallel fibers appear to be well suited for acting as delay lines since they are some of the slowest conducting axons in the nervous system. However, unlike most slow fibers, the parallel fibers cover relatively large distances. For instance, a chain of parallel fibers from one side of the cerebellum to the other (another oddity of cerebellar anatomy is that some fibers are continuous across the midline) may extend a distance of 100 mm. Since the conduction velocity within these fibers is approximately 0.5 mm/sec. (Braitenberg and Atwood, 1958), this 100 mm. chain could provide a delay signal of about 200 ms.

Depsite the elegance of the theory, Braitenberg has since come to view the basic conception of simple delay lines as inadequate due to some neurophysiological observations. Primarily, the problems lie in the fact that the results of Oscarsson (1980) have shown that somatotopic representations within the cerebellar cortex tend to cover much shorter distances (i.e. some as small as 1 mm for the entire cat) and thus the maximum delay line which can be acheived in this distance is too small to be meaningful in motor coordination (Fahle and Braitenberg, 1984). Nonetheless, Braitenberg in this most recent paper is not dismissing the role of timing entirely, but rather believes some higher order derivative may be the true computational output of the cerebellar cortex. The proposed computation is that the cerebellum matches the dynamic characteristics of movement to minimize the mechanical waves generated by the muscular contractions. Thus the computation of time is still essential, but only perhaps implicitly as one of the variables of velocity detection. In the same spirit, Pellionisz and Llinas (1982) have argued that the cerebellum can be viewed as a neuronal device for jointly mapping space and time onto a common dimensional space.

While the preceeding arguments were based on anatomical observations, many clinical and experimental results can also be interpreted as supportive of the hypothesis that the cerebellum may function as a timing device. The pioneering work of Holmes (summarized in Holmes, 1939; see also Dichgans and Diener, 1984) identified two of the more common symptoms of cerebellar dysfunction: dysmetria and dysdiadochokinesia. Dysmetria describes the inability to successfully point at a designated target. Following lesions of the cerebellar hemispheres or the deep cerebellar nuclei, particularly the lateral zones and the dentate nucleus, the patient's movements are usually hypermetric, that is, they tend to overshoot the target. Dysdiadochokinesia is generally seen in these same patients. This term describes the inability to rapidly alternate between a pair of movements involving antagonist muscles such as pronation and supination of the arm (see Eccles, 1977?). Both of these cerebellar signs have been interpreted as being the result of a breakdown in the patient's ability to time the onset and offset of the antagonist muscles. For instance, the hypermetric movement overshoots the target because the muscular activity is not properly terminated.

Evidence from researchers using electromyography (EMG) supports this hypothesis (Hallett et al, 1975; Marsden et al, 1977). Hallett et al (1975) examined the EMG records of patients who had incurred various forms of cerebellar lesions over a range of movements. They found that cerebellar patients did not tend to show any deficit in making smooth, slow movements which only required the continuous activation of the agonist muscle. However, when the same movements were made ballistically, almost all of the patients showed EMG abnormalities. In

general, the EMGs associated with rapid movements appeared normal in terms of the initial onset of the agonist burst. However, the duration of this burst tended to be longer than normal. In addition, the onset time of the antagonist and the duration of the antagonist were also disturbed. Marsden et al (1977) have reported similar results concerning the duration of both the agonist and antagonist burst. Lengthening of either the duration of the first agonist burst and/or an increase in the delay of the antagonist burst could account for both dysmetria and dysdiadochokinesia.

Animal models have further demonstrated that dysfunction in either the cerebellar hemispheres or deep nuclei can disrupt the kinematics of rapid movements (Conrad and Brooks, 1974; Beaubaton and Trouche, 1982; Vilas and Hore, 1980). These results have also tended to show that permanent or temporary lesions tend to be more disruptive for the antagonist response, the muscular burst which is assumed to provide the braking force in rapid movements. Vilas and Hore (1980) have even attempted to account for the intentional tremor seen in cerebellar patients on the basis of disruption in the braking system. The cerebellar subject is assumed to have lost the capacity for anticipating when to initiate the braking process and thus becomes dependent on afferent input in order to trigger the antagonist response. Thus the antagonist appears later than normal. Furthermore, a second agonist burst which is presumed to serve as a damping mechanism is similarly delayed and thus a series of oscillations, the intentional tremor, is produced.

One final line of evidence that the cerebellum is involved in timing functions comes from the recent work of Thompson and his colleagues in the area of motor learning (reviewed in Thompson, Clark, Donegan, Lavond, Lincoln, Madden, Mamounas, Mauk, McCormick, and Thompson, 1984). These researchers have carefully established that the integrity of certain structures within the cerebellum are essential in the development of conditioned responses in classical conditioning. Their studies lead them to believe that the interpositis/dentate nuclei paly a critical role in the storage of the conditioned response (but see Yeo et al, 1985a; 1985b). Moreover, they have also found that lesions of the cerebellar hemispheres may not abolish the conditioned response, but may seriously disrupt the timing on this response (McCormick and Thompson, 1984). It is important to keep in mind that the onset of the CR is linked to the onset of the aversive stimulus (US) which follows the CR rather than being linked to the CS which preceeds the CR. The anticipatory nature of the CR strongly suggests explicit timing and the disruption of the timing of the CR following lesions of the cerebellar hemisphere further supports the hypothesis that the cerebellum plays a primary role in timing.

It should be made clear, though, that the abnormalities in the EMG profile and the conditioning results can only be viewed as indirect evidence for timing deficits. Alternative explanations which do not involve a timing mechanism could be invoked to account for these results. For instance, one might speculate that the onsets and offsets of the EMG bursts are regulated by feedback from the periphery. Cerebellar lesions may disrupt the required feedback loops and this may lead to the observed abnormalities. Another alternative is that the reciprocal EMG activity commonly observed in ballistic movement is controlled without any explicit timing. It is hoped that our experimental tasks provide a more direct test of timing functions.

Method

Subjects:

In this preliminary report, we will only provide a summary description of the neurological evaluation of the different patients. The authors were assisted at all times by a number of neurologists who performed clinical testing and, when available, CT scan reports.

Parkinson's Disease patients: The Parkinson patients can be separated into three, distinct groups: The Eugene group (n=12, mean age=66.8, sd=8.8) and the German group (n=11, mean age=58.0, sd=9.9) were all tested with the same protocol, the only difference between the groups being that the location was different and that the latter group was instructed with the aid of an interpreter. All of these subjects were tested without any changes in their normal medication schedule. The On-Off group (n=7, mean age=65.1, sd=7.9) was tested in two separate sessions: Once in which they were in their normal medication cycle and once in which they had skipped their morning medication periods. Four of these subjects were first tested when they were "off" medication and the other three were first tested when they were "on" medication. Each session was usually separated by one week.

Cortical patients: The cortical patients were tested in Germany (n=8, mean age=58.4, sd=7.9). They had all incurred lesions which extended into the posterior region of the frontal lobe. All of these subjects showed some hemiparesis on the side contralateral to the lesion. There was no clinical or radiological evidence that any of these patients had damage in any subcortical regions.

Cerebellar patients: There were a total of 22 cerebellar patients (n=22, mean age=45.7, sd=16.1), of which 19 were tested in Germany. Most of the subjects (n=16) in this group had been diagnosed as showing signs of cerebellar atrophy on the basis of clinical examination and/or CT records. The degree of atrophy varied from mild to severe and in some cases, the atrophy was suspected to have extended into nuclei that project to the cerebellum (e.g. olivo-ponto-cerebellar atrophy). The remaining cerebellar patients had incurred either vascular accidents within the cerebellum (n=5) or had undergone surgery for the removal of a cerebellar tumor (n=1). We have tested other patients for whom the primary diagnosis was cerebellar ischemic lesion, but have excluded these patients because there was some evidence that the damage had extended into brain stem structures.

Peripheral neuropathy patients: This group included 4 subjects (mean age=55.8, sd=18.8) who had experienced some moderate impairment of their hand coordination due to peripheral nerve damage. Two of these subjects had ulnar nerve damage, one medial nerve damage, and one had suffered a pinched nerve at the level of the shoulder. In some of these patients, the neuropathy had produced muscular atrophy (see Ivry and Keele, 1985 for a more thorough discussion of one of these patients). Our criterion for this group was not so much based on the type of peripheral neuropathy, but rather that the subject experienced some difficulty in making finger movements due to a deficit which did not involve subcortical or cortical structures.

Sensory loss patient: One subject (age=61 years) who was functionally deafferented below the level of the elbow on the right side. The polyneuropathy was the result of mercury poisoning and had produced complete loss of all deep and surface sensation. Motor functions appeared to be normal except for some

mild atrophy of the small hand muscles. The left arm of this patient had been amputated and thus we were not able to make any within subject comparisons.

Epileptic subjects: The epileptic subjects (n=29) were tested on the perception tasks only. These tasks were included in a battery of neuropsychological testing conducted as part of the assessment procedure to determine the effects of temporal lobectomy surgery on perceptual and cognitive functioning. The patients are thus severe, chronic epileptics in which the seizure disorder has a primary focus in the temporal lobe. 16 of these subjects were scheduled or had undergone a left temporal lobectomy and the remaining 13 had a right-sided disorder. The mean age of these subjects is not presently available, but almost all of these subjects are between the ages of 16 and 30. Some of the epileptic patients were tested both before and after surgery. No differences were obse- -d and thus only the first score obtained from each subject will be reported. Some of the subjects were only tested post-surgery.

Control subjects: Two groups of control subjects were tested. One group was composed of college age students (n=24) who volunteered for the experiment in order to fulfill requirements for psychology courses at the University of Oregon. All of these subjects were below the age of 25. The other group was composed of subjects who were above the age of 50 (n=10, age=65.0, sd=9.5). All of these subjects reported a medical history which was free of any neurological problems. These subjects were paid $5 per hour. (Any patients tested in Oregon were also paid $5 per hour. The German subjects were not paid.)

Procedures:

The tasks which were used in these experiments have all been used in previous experiments (Keele et al, 1985a; Pokorny, 1985; Keele et al, submitted). The reader is advised to consult these manuscripts for detailed descriptions of both the methodologies and the underlying logic supporting each methodology. A brief description of the tasks will be provided here.

1. Production of time (Tapping Task): The subject was seated with the arm used for tapping resting on a table, palm down. The subject placed the designated effector on the left most microswitch mounted on a wooden block. The designated effector was usually the index finger of the subject's dominant hand unless the neurological deficit dictated otherwise (i.e. the affected hand was the non-dominant hand for lateralized patients). Pressing the microswitch provided a pulse to an Apple II computer which recorded all responses to the nearest millisecond.

Each trial began with a series of 50 ms. tones (65 dB. (A)) which were presented at regular intervals of 550 ms. This pace is 100-150 ms. slower than the pace which we have used in most of our previous experiments. However, pilot work with Parkinson patients showed that the faster paces might approach their maximal tapping rate. The subject was instructed to begin tapping along with the tones once he had internally established the desired pace. After the subject's first response, 12 more tones were presented during which time the subject attempted to synchronize his responses. The subject was instructed to continue tapping at the same rate when the tones ended. After 31 self-paced taps had occured, the computer signalled the end of the trial and feedback was provided indicating the mean interval produced with and without the tones and the standard deviation of the inter-response-intervals (IRI).

Each block of trials was concluded once the subject had produced either six acceptable trials (sequence of 12 paced and 31 unpaced responses) or six unacceptable trials. A trial was considered unacceptable if any IRI was less

than or greater than 50% of the base duration (less than 275 ms. or greater than 825 ms.). The data from these trials were excluded from subsequent analysis. This is an criterion which we have adopted in our previous research with normals since such deviant values could be due to either tremor or insufficient force to register a response. All subjects performed in at least two blocks of tapping trials and many (noted in the results section) participated in additional blocks.

Our analysis of the tapping data is based on a theoretical model of the timing of repetitive movements that was developed by Wing and Kristofferson (1973). The model postulates that the variability of the IRIs will arise from two independent sources: a central timekeeper and the motor implemenatation system. In other words, the total variability observed in the tapping task is the sum of random variation in the timing mechanism which signals when a response should be initiated and variability in the implementation system which executes that command. These two processes are assumed to operate independently of each other. They are further assumed to be independent random variables with normal variances signified by θ^2_c (c for clock) and θ^2_{md} (md for motor delay).

Figure 2a depicts these processes in a hypothetical series of responses in which the variability of the timekeeper is zero. Each IRI is thus the sum of a timekeeper interval plus the difference in motor delays associated with the initiation and termination of that response:

$$I_j = C_j + MD_j - MD_{j-1}$$

Since the two sources of variance are independent, it follows that :

$$\theta^2_I = \theta^2_c + 2\theta^2_{md}$$

(1). θ^2_I is directly obtained from the subject's data. It is the variance of all responses around the subject's generated mean interval (which is expected to drift only slightly). The essence of the Wing and Kristofferson (1973) model is that both of the two sources of variance can be estimated from the covariance function of the series of responses. In short, a randomly large motor delay will produce both a long preceding response and a short following response (as shown at I3 and I4 in Figure 2a). It is important to note that this follows because the delays are independent of the timekeeper pulses and are not the result of any feedback process. That is, motor delay variation involves a negative covariance between successive intervals, and the magnitude of that variance serves to estimate motor delay variance (2). Figure 2b, which depicts an analagous series of taps in which θ^2_{md} equals zero, shows that there is no similar dependency between successive intervals as a function of imprecision in the timekeeper. Thus, an estimate of θ^2_{md} is obtained from the lag one autocovariance, or more specifically:

$$\text{autocov}(1) = -\theta^2_{md}$$

A final product of the model is that the covariance of all subsequent lags should be zero.

This two-process model of periodic movement has received support from a number of different paradigms. First, of critical importance, is the finding that the model accounts well for th general autocovariance functions produced by normal subjects. The correlation between successive intervals is almost always negative as predicted (Wing and Kristofferson, 1973) whereas the covariance for lags greater than one is minimal. Second, Wing (1980) reported that only the estimate of the timekeeper variability was related to the duration of the base

interval. This is predicted from the model since only the frequency of the timekeeper is adjusted following changes in the base duration, whereas the motor delay is assumed to be constant.

2. Perception Tasks: All of the perception tasks (duration, loudness, and [illegible] used the same threshold procedure developed by Lieberman and Pentland (1982). The Parameter Estimation by Sequential Testing (PEST) procedure determines the upper and lower thresholds for a given criterion. In short, the advantage this method provides over standard threshold methods (e.g. the method of constant stimuli) is that the subject's previous responses are used in calculating the test values to be presented on each trial. Unlike our previous study (Keele et al, 1985a) in which the threshold was defined as one standard deviation from the point of subjective equality assuming the logit distribution, we adopted a criterion of 1.5 standard deviations in the present experiment. Thus the thresholds are approximately located at points along the logit distribution at which the subject is correct on approximately 90% of the trials. This new criterion was adopted in order to make the two threshold points more discriminable for the subjects. Simulation testing showed that the estimated thresholds were at least as stable with this criterion as with our previous criterion of one standard deviation. The difference between the upper and lower threshold points were used as measures of perceptual acuity. For most of the groups these estimates were based on 25 judgements for the upper threshold and 25 judgements for the lower threshold.

2a. Time perception: Subjects compared successive intervals generated by two pairs of tones. Each tone was 50 ms. in duration, played at a [illegible] of 73 dB (A), and at a frequency of 1000 Hz.. The onset-to-onset interval between the first pair of tones was always 400 ms. One second after the offset of the first pair, the second pair was presented. On half the trials the interval between the second pair of tones was chosen in order to estimate the lower threshold (i.e. the point at which the subject would correctly respond "shorter" on 90% of the trials) and on the other half of the trials the upper threshold was sampled (i.e. the point at which the subject would correctly respond "longer" on 90% of the trials). The logit distribution was divided into 61 equal steps with 6 ms. between each step.

2b. Loudness perception: This task was included in order to serve as a control for general auditory deficits. That is, difficulty in the time perception task may not be the result of a specific deficit in the timing process, but rather, may reflect a general inability to process auditory stimuli. If this were so, those subjects who perform poorly in the time perception task should also have difficulty in making loudness judgements. The procedure was similar to the time perception task in that each trial involved two pairs of tones separated by one second. The tones within each pair were always separated by 400 ms. and the duration of each tone was 50 ms. played at a frequency of 1000 Hz. The volume of the two tones in the first pair was 73 dB (A), whereas the volume of the second pair varied. The subject judged whether the volume of the second pair was louder or softer thatn the standard. As before, the logit distribution was divided into 61 steps with approximately 0.27 dB (A) between each step.

2c. Frequency perception: This task was included as the auditory control in our testing with one group of subjects, the temporal epilepsy group. The procedure was identical to that used in the other two perception tasks except

that the second pair of tones varied in frequency as opposed to either duration or loudness. Each of the 61 steps were separated by 1.16 Hz.

3. Force Control: Many of the subjects were also tested on a force control task. The results of this part of our research will be reported in other publications. Details of this task can be found in Keele et al (submitted). The task requires the subject to make finger presses on a response button situated over a force transducer. Each subject used the same finger in this task as was used in the tapping tasks.

Order of tasks:

Due to time limitations with the German patients and the Portland epileptic patients, we chose to adopt a flexible strategy in sequencing the various tasks. For instance, patients with peripheral neuropathies or those who had lesions restricted to only one side were run extensively on the tapping task since we could then test both the affected and unaffected hand in order to obtain within subject control data. These subjects might not then have ever been tested on either the perception or force tasks. The epileptic patients, on the other hand were only tested on the perception of time and frequency tasks, the order being counterbalanced across subjects.

Most of the subjects, however, were initially tested in one of three basic protocols. The first protocol was composed of: Tapping 1-- Time Perception-- Force 1-- Loudness Perception-- Tapping 2-- Force 2. Subjects tested with this protocol included the elderly control group, all of the Eugene Parkinson group, most of the German Parkinson group and cerebellar patients, and some of the cortical patients. The order was the same for all subjects tested with this protocol and the session took approximately 1.5 hours. Some of these subjects participated in additional testing sessions in order to obtain more tapping data.

The second protocol was composed of: Force 1-- Tapping 1-- Force 2-- Time Perception-- Tapping 2-- Loudness Perception-- Force 3-- Tapping 3-- Force 4. The On-Off Parkinson group was tested with this protocol with a single session taking approximately 1.45 hours. The third protocol involved: Tapping 1-- Time Perception-- Tapping 2-- Loudness Perception-- Tapping 3-- Frequency Perception-- Tapping 4. The College-Age control group was tested with this protocol, each session only taking 1 hour.

It will be noted that, except for the epileptic subjects, we did not attempt to counterbalance the task order, but instead relied on constant protocols. We felt this was most advisable due to the heterogeneity within each group and because our most interesting comparisons are between groups. It is important to note, though, that in all three protocols, the perception of time task preceded the perception of loudness task.

Results

In the statistical analyses to be reported below, we have employed t-tests in order to compare the scores from the different groups. We recognize that this may not be the most appropriate statistic, especially since the large number of comparisons will greatly increase the probability of Type 1 errors (falsely rejecting the null hypothesis). However, this statistic is easily applied when there are an uneven number of subjects in the different experimental groups. It is also appropriate in a preliminary stage of experimentation when one wants to maximize the detection of differences that can then be confirmed in subsequent studies. We do wish to stress, however, that in this preliminary report we are more interested in the general pattern of results, rather than in making any strong claims based upon formal analyses.

Tapping results:

Before examining the tapping results, we need to point out two procedures which were applied to the raw data. The first was designed to minimize the increase in the variability estimate which would occur if a subject's responses tended to drift away from the base interval. To do this, a regression line was fitted through the 30 intervals produced by the subject and the variability was calculated in terms of the deviation of each response from this trend line. This correction has the effect of slightly increasing the motor delay estimate since it minimizes the positive correlation between successive responses which is observed when the subject's subjective base interval is either lengthening or shortening.

The total variability score for each subject from a block of six successful trials was then decomposed into separable estimates of the timekeeper and motor delay components. This procedure yielded some scores which appeared to indicate that certain assumptions of the Wing and Kristofferson (1973) model had been violated. Generally, this involved a Lag 1 covariance estimate which was positive. Wing (1977) has proposed four alternative models which may provide more accurate estimates of the timekeeper and motor delay estimate when the assumptions of the basic model are violated. However, the data did not indicate that any of these models were more valid than the basic model, and thus we have assumed that the violations may best be attributed to the relatively small data set of six trials per block. This led us to subsitute a motor delay estimate of zero whenever the Lag 1 covariance estimate was greater than zero and assume that all of the variability was due to the timekeeper process. Note that if we did not make this subsitution, the estimate of the timekeeper variability would be greater than the total variability, a nonsensical result.

In our control groups, the percentage of violations of the basic Wing and Kristofferson model was 14.7% (12.5% for the college aged subjects and 20% for the elderly control group). Most of these involved Lag 1 covariance estimates which were minimally above zero. The patients tended to show a different pattern of results. The peripheral neuropathy patients rarely demonstrated any violations (2% of all blocks) whereas the other patients produced Lag 1 estimates which were greater than zero on 20.3% of the blocks. The percentage was never higher than 25% (the German Parkinson group) and was similar for each of the cortical and subcortical groups.

Table 1 presents the results for each control and patient group tested on the tapping task. Before turning to the main data of interest, a few points should be made. First, as can be seen in the second column, all of the groups

produced mean intervals which were slightly shorter than the given pace interval of 550 ms. This tendency is most apparent with the Parkinson patients, with some of these subjects averaging under 500 ms. At present we do not have any strong insights concerning this finding (and it is not consistent across subjects). We have explored the possibility that this tendency to speed up may be related to the resting tremor exhibited by the Parkinsonians, but some tests of this hypothesis have not been supportive (unpublished data).

Secondly, there were three patients in the cerebellar group and one in each of the German Parkinson and cortical groups who were unable to complete the task. That is, they were unable to produce a series of 31 responses in which all of the intervals were within +-50% of 550 ms. It can be assumed that these subjects would have increased the variability scores in their respective categories if we had not included our arbitrary criterion.

The third column of Table 1 presents the mean standard deviation of the IRIs for each group. The fourth and fifth columns show the partitioning of this overall variability score into separable estimates of the variability associated with the timekeeper and motor delay processes, respectively. The two control groups demonstrate that there is a considerable increase in variability as a function of age ($t(32)=4.60$, $p<.05$). Furthermore, this increase appears to be entirely attributeable to increased variability in the timekeeper process ($t(32)=4.20$, $p<.05$). A similar comparison of these groups motor delay estimates revealed no differences ($t(32)=0.43$). (But see Keele et al, 1985a for a similar study in which a different pattern of results emerged.) Not suprisingly, the performance of the college age group was superior to that observed with all of the patient populations.

The results of the peripheral neuropathy group provide a critical test of the validity of employing the Wing and Kristofferson method in neuropsychological testing. A strong prediction of the model is that any deficit that these patients have should appear as inflated motor delay estimates since the neurological damage is in the implementation system. As noted earlier, the timing processes are assumed to operate independently of the implementation system. The results for the four peripheral patients are highly supportive. The clock estimate for this group is slightly lower than the elderly control group whereas the motor delay estimate is almost 70% nigher. This predicted dissociation leads us to believe that the Wing method can be useful in trying to identify the neural mechanisms involved in timing.

In a much weaker sense, the data from the one functionally deafferented patient is also supportive of the assumption that feedback is not involved in determining the clock cycle. This inference is based on the observation that this subject's performance was quite similar to that observed in many of the healthy elderly subjects. The motor delay estimate of 13.2 is lower than the scores for four of these control subjects, but may still reflect some slight disruption in the implementation pathways. Nonetheless, performance is at least moderately good.

Of primary interest are the results of the subcortical and cortical groups. The results for the three different Parkinson groups are remarkable consistent. Since there were no statistical differences between these three groups, their data were pooled in subsequent analyses. As can easily be seen in the table, the Parkinson patients performed at least as well as their age matched control group. This finding is even more striking for the On-Off group since the results

presented in Table 1 are from the test session in which the subjects had forgone medication for approximately 12 hours.

The cortical and cerebellar groups, however, were much more variable in the tapping task than both the Parkinson patients ($t(41)=3.96$, $p<.05$ for the cerebellars; $t(34)=2.57$, $p<.05$ for the corticals) and the elderly control group ($t(22)=2.79$, $p<.05$ and $t(15)=2.81$, $p<.05$ for the cerebellars and corticals, respectively). In both of these groups, the mean estimates of clock and motor delay variability following the Wing decomposition is increased in comparison to the Parkinson patients and elderly control subjects. The statistical analyses of these results, however, are not as straightforward and should be taken with a large grain of salt considering the small number of subjects in the cortical and control groups. In terms of the clock estimate, the cerebellar group performed significantly worse than both the elderly control group ($t(22)=2.0$, $p<.05$) and the combined Parkinson group ($t(41)=2.75$, $p<.05$). The clock estimate for the cortical group does not differ significantly from either comparison group ($t=1.24$ in both cases). On the other hand, the cortical group has a higher motor delay estimate than both groups ($t(15)=1.86$, $p<.05$ for the control; $t(34)=2.30$, $p<.05$ for the Parkinson) whereas the cerebellar patients are only significantly more variable on this component than the Parkinson group ($t(41)=2.04$, $p<.05$).

We strongly suspect that both the cerebellar and cortical patients will have reliably higher clock and motor delay estimates than both the control and Parkinson patients when the number of cortical and control subjects is increased. We are presently in the process of testing more of these two types of subjects in order to make the number of subjects more equal across the different groups.

In summary, the group results of the tapping task indicate that both the cortical and cerebellar patients are more variable in making periodic responses. This increased variability is attributed to increased noise in both the clock and motor delay components according to the Wing and Kristofferson model. Moreover, at present there are no differences between the estimates for these two groups on either the clock ($t(19)=0.84$) or the motor delay ($t(19)=-.11$) components. It is unclear whether these differences would approach significance if the number of subjects in each group was increased.

In addition to the group data, we have also examined some subjects from each of the four neurological groups who presented the opportunity for making within subject comparisons. This group was mostly composed of patients who showed large clinical differences between two effectors. We have included most of these subjects' performance with their most affected hand in the group data reviewed above. However, in a couple of instances in which a very different methodology was used (e.g. earlier research in our laboratory which was not conducted by RBI), these subjects are only included in the within subject analysis.

The usual procedure employed with these subjects was to alternate testing on the tapping task between the index finger of the affected and unaffected hand. We have never found any differences as a function of handedness in this task nor have we found any differences between performance with the hand in comparison to the foot (Keele et al, 1985a). Affected-unaffected index finger comparisons were made with seven cortical patients, five cerebellar patients, three peripheral neuropathy patients, and three Parkinson patients.

There were three other types of within subject comparisons which will be included in this section. First, the peripheral neuropathy subject with medial nerve damage was asked to tap with either the thumb, middle, or little finger on her affected hand. The medial nerve is primarily a sensory nerve, but also has a

motor function in terms of its innervation of the little finger. For this subject the performance with the thumb and middle finger was pooled to serve as the control data. Secondly, a 76 year old man was admitted to the clinic in Germany to begin treatment for Parkinson's Disease. This provided the opportunity to observe his performance on the tapping task before he had received any medication and then track his performance over the first two weeks of medication. The within subject comparison here is thus pre- versus post-medication. Third, we will report in this section the performance of the On-Off Parkinson group under both testing conditions. It should be noted that all of these patients had been receiving L-Dopa for over 10 years and "Off" medication merely refers to their willingness to skip the first couple of medication periods on the test day.

The results of these single subject mini- experiments are pooled by subject group in Table 2. The top row for each group indicates their performance in the unaffected condition and the bottom row shows their scores when tapping in the experimental condition. Almost all of the subjects included in this table completed between four and eight blocks of six tapping trials with each effector. Thus, the data are considerably more stable than in the preceding section in which most subjects only completed two blocks.

The results are in close agreement with that found in the group comparisons. The peripheral neuropathy patients consistently show increased variability when tapping with the affected finger and this increase is solely assigned to the motor delay component. As was also seen in Table 1, the cortical and cerebellar patients show increased estimates in both the clock and motor delay estimates when tapping with their affected hand. Note that in both of these groups, performance with the unaffected hand tends to approximate normal performance, although there may be a slight increase in the motor delay estimate. Nonetheless, these subjects clearly show a deficit in both the clock and implementation processes.

The results for the Parkinson subjects are more problematic. The On-Off comparison shows minimal difference as a function of medication extending the earlier observation that basal ganglia deficits do not affect performance on this task. However, the four other Parkinson subjects show a decrement in performance when tapping in the affected condition (bad hand or pre-medication). While there is little difference between the motor delay estimates, the Wing and Kristofferson analysis indicates that the problem stems from increased variability in the timekeeper process. The largest asymmetry in this group is due to data of MF, a subject whose performance has previously been reported in Wing et al (1984). This subject shows a 114% clock increase when tapping with her affected hand. However the three other subjects show increased clock estimates of 55%-70%. It is difficult to reconcile the divergent results observed with the Parkinson patients. The group data indicates that these patients are unaffected in the tapping task whereas these special cases show that the integrity of the basal ganglia may be necessary for normal functioning of the timekeeper processes. We have not been able to account for these findings by classifying patients into the subcategories (e.g. those who are rigid, or have tremor, or are bradykinetic) of Parkinson's Disease cited in the literature (DeLong and Georgopoulos, 1981).

Perception results:

Tables 3 and 4 present the results from the perception tasks. Table 3 shows those groups in which the perception of loudness was included as a control for

general auditory deficits. The perception of frequency was used as a control with the epileptic patients and the results for this group are shown in Table 4. The mean scores represent the number of steps between the upper and lower thresholds. These thresholds correspond to the points on the logit distribution at which the subjects are making the correct response on approximately 90% of the trials. Each step in the duration task corresponds to 8 msec., 0.27 dB (A) in the loudness task, and 1.16 Hz. in the frequency task.

As seen in the tapping data, the results appear to indicate that there is some decrease in acuity as a function of age in normal populations. However, only the volume task yielded a reliable difference between the elderly control group and the college age group ($t(32)=1.75$, $p<.05$). There was no significant difference between these two groups on the perception of duration task ($t(32)=0.84$). The two perception tasks can be assumed to measure separate processes since there is no correlation between performance on them with the healthy control groups (-.06 for the elderly group; .14 for the college age group).

The results shown in Table 3 can be summarized quite easily. Only the cerebellar group shows a deficit in the perception of duration task. The mean scores for the cerebellars and the elderly control group are not significantly different ($t(26)=1.26$). Since there are no statistical differences between the means of the various Parkinson groups on either the duration or loudness task, their scores were pooled. The cerebellar group was significantly impaired on the perception of duration in comparison to the pooled Parkinson group ($t(44)=1.70$, $p<.05$). Additionally, if the Parkinson group is combined with the elderly control group (since these two groups did not differ), the cerebellar group is also significantly worse in the time perception task than this summed group of elderly subjects ($t(54)=1.96$, $p<.05$). No comparisons were made with the cortical group because of the small number of cortical patients who have presently been tested in the perceptual tasks.

It is important to note that the cerebellar deficit in the perception of duration task can not be attributed to some sort of general auditory deficit associated with cerebellar disorders. In fact, the cerebellar group performed slightly better that both the elderly control group and the pooled Parkinson patients in the perception of loudness task.

Table 4 is of interest because of the occassional speculations in the literature that the temporal lobes, particularly the left temporal lobe plays an important role in timing functions (Effron, 1963; Carmon and Nachshon, 1971; Tallal and Newcombe, 1978; MacKay, 1985). Some of these hypotheses have attributed an explicit timing role to the temporal lobes whereas other ideas have emphasized the sequential nature of left hemisphreric function. Sequencing processes may only require the ability to maintain temporal order rather than control some form of real-time metric as we assume is required in our tasks. The results of our testing severe temporal lobe epileptics show that these patients do not have any deficit in making duration judgements. This result holds for patients in which the seizure focus is in the left or the right temporal lobe. This finding is somewhat suprising given that some of these patients are intellectually impaired and have some memory disorders (John Walker, Good Samaritan Hospital, personal communication). Unexpectedly, the epileptics did appear to be impaired in the perception of frequency task. These differences, however, were not reliable due to the large variability in both the epileptic and control groups.

Discussion

Previous work in our laboratory (Keele et al, 1985a; Keele et al, submitted) has led us to postulate the control of voluntary movement may involve the use of an internal procedure which controls timing functions. For instance, we have found that people who are good at maintaining a rhythm with one effector are also good at periodic tapping with a different effector. Furthermore, the ability to produce regularly timed intervals was found to correlate with the ability to accurately perceive intervals of a comparable duration. These findings have been interpreted as demonstrating the existence of an internal timekeeping process.

One of the main purposes of the present research is to try to identify those neural structures which are part of this timekeeping process. The logic is relatively straightforward. The notion of an internal clock suggests that specific neural systems may be organized in such a manner as to function as a timing device. Damage to these neural systems would be expected to lead to difficulty in tasks which involve the timing mechanism. On the other hand, we have no a priori reasons to expect the timing processes to be strictly localized. Thus, the use of neurological patients is useful, not only as a means of further investigating the existence of timing processes, but also as a way of uncovering the nature of those processes. While localization can be of considerable interest in and of itself, we have viewed neuropsychological testing as a means of providing a converging operation to supplement our correlational and experimental work.

At present, the results of our patient work are extremely promising. As a starting point, we believe that the Wing and Kristofferson model of repetitive movements provides a useful theoretically-based tool for studying timing. While their model has been exploited with normal populations, the extension to patient groups has not been systematically tested. The results with the peripheral neuropathy group are very convincing. As predicted by the model, only the estimate of the implementation portion of the variability was found to increase following peripheral nerve damage. This dissociation demonstrates that the source of a deficit in tapping performance can be successfully identified through the Wing and Kristofferson (1973) model.

The results of the tapping task with the various cortical and subcortical groups may at first glance appear quite problematic, and indeed, we do not believe any definitive answers can yet be garnered. Nonetheless, we believe the results can be accomodated within the present understanding of the neuroanatomical connections between the various motor systems of the brain. A simplified wiring diagram is provided in Figure 3 (adapted from Keele et al, 1985b). In this diagram we focus on the position of the basal ganglia and cerebellum in relation to the motor cortex and spinal systems.

The first point to be made is that most of the direct projections down the spinal cord originate in either the primary motor cortex or the cerebellum. These are commonly referred to as the pyramidal and extrapyramidal tracts, respectively. There appears to be little output from the basal ganglia which can have such direct (1 or 2 synapses) influence on the spinal neurons. This arrangement nicely meshes with our finding that both the cerebellar and cortical patients may produce inflated motor delay estimates. At least part of the lesioned tissue is presumably outside of the timing system and part of the implementation pathways. More interesting, in none of our Parkinson groups nor

in the few Parkinson patients who had difficulty in the tapping task have we ever found any increases in the motor delay scores.

We propose, however, that the three neural systems examined in this study are either part of a timing loop or nested within a circuit in which the cerebellum plays a primary role in timing. A loop- or circuit-based hypothesis is necessary to account for the fact that damage in either the cerebellum, cerebral cortex, or the basal ganglia can increase the variability of the timing process. The independence assumption of the Wing and Kristofferson model implies that any system which was not contained within the timing process could only affect the motor delay estimate.

We can imagine at least two different types of timing circuits. The first type would implicate all of the different structures within the circuit in the control of timing. Thus, the timing of say 400 ms. would involve setting up a path through the loop which takes 400 ms. to circuit. 500 ms. paths would presumably involve more synapses or slower conducting neurons in order to increase the amount of time it takes to complete each circuit. Damage at any point along the circuit would disrupt the normal functioning of this type of clock. There are a number of problems with this type of mechanism. For one thing, the pathways involving the basal ganglia and the cerebellum presumably do more than just provide long delay lines. Yet this notion of loop timing seems to presume that the actual circuits traversed throughout the entire motor pathways are determined on how much delay they contribute to the overall transmission time. Secondly, there is little communication between the cortical-basal ganglia loop and the cortical-cerebellar loop (despite the common projection of both subcortical structure in the ventral lateral portion of the thalmus) and thus the circuit can not really be continuous (e.g. Goldberg, 1985). Furthermore, it is difficult to construct such a mechanism without postulating some sort of control system which determines the circuit of the loop. A loop traversing such diverse structures needs to be controlled by a system operating at a very global level. On the grounds of plausibility it seems reasonable to argue for distributed, local operations whenever possible.

The second form of a timing circuit captures this property quite well. What we are proposing is that the cerebellum plays a primary role in timing in the spirit of the millisecond timer proposed 25 years ago by Braitenberg. Cerebellar subjects show substantial increases in that portion of the variability attributed to the timing process in the tapping task. More surprising, they are the only group which showed any deficit in the perception of time tasks. This timing function of the cerebellum, though, is still contained within the circuit which in its entirety constitutes the motor program. Thus, the cerebellum serves as a subroutine which computes the timing requirements for a motor program.

In addition to the results with the cerebellar patients, we have also observed that cortical lesions produce timing deficits as well as certain basal ganglia disorders. We believe our present model can accomodate these results. For the sake of argument, imagine that the motor cortex has just sent a signal down the pyramidal tract which triggers a key press. This signal then initiates the process needed to determine the next response, i.e. the establishment of the next motor program. The various procedures (subroutines) are thus invoked. For instance, the cerebellum is called upon to determine the time at which the response can be made and the basal ganglia provides some other (unknown) parameter input. (3) When all of the computational outputs of the various subroutine are returned to the motor cortex, the next response is triggered.

Once this occurs, the cycle is repeated and each procedure is again executed. The important point to note from this simplified example is that deficits which affect any of the subroutines or disrupt the system at any point prior to the triggering of a response will contribute to increased timing variability. The affected structures may not play any role in timing control, but they can induce added noise in the timing circuit since the different subroutines can not be called until the preceding response has been initiated.

Of course, the results from the tapping task do not differentiate between the cortical and cerebellar systems in terms of the locus of timing control. Clinical symptoms and previous experimental work, as well as Braitenberg's theory had pointed us in the direction of the cerebellum as a timing device. The results of the perception of time task further support this idea. It is important to note that the perception of loudness task emphasizes that the cerebellar deficit can not be considered a general deficit in auditory perception, but rather, that the perceptual deficit is specific to timing. In fact, we know of no previous work which has shown perceptual deficits associated with cerebellar lesions, despite the massive input to the cerebellum from sensory pathways.

Taken together with the tapping results, the results from the time perception task support our earlier hypothesis (Keele et al, 1985a) regarding the existence of a common timing mechanism which is involved in both the production and perception of time. We believe that these results represent an important step in developing the concept of the motor program. The motor program is defined at a global level in terms of an abstract representation. However, it is composed of a number of distributed procedures which can be employed in the performance of a wide range of coordinated behaviors.

Despite the overly optomistic flavor of this discussion, we feel obliged to conclude by emphasizing that these results must be considered preliminary. Our primary impetus for this stems from the suprising finding that only the cerebellar patients showed a perceptual deficit. We are presently setting up a replication study of this work. This seems especially appropriate given that there are a number of methodological differences between the testing procedures used with the various patient groups. For example, almost all of the cerebellars were tested in Germany with the assistance of an interpreter whereas some of the Parkinson patients and all of the control subjects were tested in Oregon.

Moreover, at present, we have only tested four cortical patients on the perception tasks. Since we have relied on the results of the perception of time task to differentiate between the corticals and cerebellars, we need to increase the sample size of the cortical group. We also need to more closely examine why some cerebellar patients primarily show motor delay deficits whereas the timing process is disrupted in other cerebellar patients. We are currently developing a hypothesis that the differences may be accounted for on the basis of the site of the lesion within the cerebellum. The prediction is that medial lesions are associated with increased implementation variability whereas lateral lesions produce clock deficits. However, our evidence for this is quite minimal. In a similar vein, we hope eventually to be able to account for the discrepant results we have observed in the Parkinson patients.

Footnotes

1. This follows since, if x and y are independent random variables,

$$\sigma^2_{x+y} = \sigma^2_x + \sigma^2_y$$

2. See Wing (1980) for a more thorough discussion of the Wing and Kristofferson model.

3. The role of the basal ganglia in motor programming is one of the main questions we are presently addressing. One possibility which we are exploring is that the basal ganglia may be important either directly or indirectly in force regulation.

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Table 1

Tapping task, group data. Given interval was 550 ms. Subjects who were unable to perform the task are indicated by subtracting number in parenthesis from listed N. SD refers to standard deviation of inter-response intervals. Clock and motor delay estimates are determined according to the model developed by Wing and Kristofferson (1973).

Group	N	INT	SD	CL	MD
Controls					
Elderly	10	544.5 (12.2)	32.2 (5.8)	26.4 (7.7)	10.5 (6.6)
College Aged	24	535.4 (11.9)	23.6 (4.6)	17.9 (4.0)	9.6 (5.0)
Parkinsons					
Eugene	12	520.2 (41.0)	31.3 (8.9)	27.8 (8.9)	8.5 (6.8)
German	10 (of 11)	531.4 (23.4)	32.3 (9.8)	27.0 (10.9)	10.0 (7.3)
On-Off	7 (off only)	521.7 (32.0)	33.6 (9.2)	27.7 (3.8)	11.8 (8.9)
Cerebellars	14 (of 17)	536.6 (18.3)	47.4 (16.4)	36.9 (15.4)	16.2 (13.2)
Corticals	7 (of 8)	543.8 (19.0)	41.7 (8.2)	31.5 (10.8)	16.8 (8.0)
Peripherals (Affected hand only)	4	535.0 (18.6)	34.0 (3.7)	23.3 (1.6)	17.0 (2.8)
Sensory Loss	1	525.8	31.3	24.9	13.2

Table 2

Tapping task, within subject comparisons. Abbreviations as in Table 1. Top line within each pair refers to performance with good effector, bottom line is for impaired effector (one Parkinson subject is pre- versus post-medication). On-Off comparison refers to chronic Parkinsonians who skipped morning medication period(s).

Group	N	INT	SD	CL	MD
Cerebellars	5	538.1	33.6	24.5	15.4
		546.5	51.6	39.3	22.8
Parkinsons					
Affected hand	4	528.7	29.3	25.6	9.4
Impaired hand		540.7	50.1	46.5	11.5
On medication	7	524.0	33.6	28.4	10.7
Off medication		521.7	33.6	27.7	11.8
Corticals	7	539.8	32.1	23.8	13.4
		541.9	42.4	30.0	18.8
Peripheral Nerve Damage	4	532.0	28.6	22.6	12.2
		535.0	34.0	23.3	17.0

Table 3

Perception tasks, duration and volume judgements. Scores are in terms of step differences between lower and upper thresholds. Standard deviations are given in parenthesis.

Group	N		Duration	Loudness
Controls				
Elderly	10		11.7 (4.7)	14.7 (7.1)
College Aged	24		9.8 (6.1)	10.8 (3.9)
Parkinsons				
Eugene	12		12.2 (7.5)	14.6 (8.3)
German	9		13.7 (7.7)	11.7 (4.1)
On-Off	7	On:	8.9 (4.0)	10.4 (2.8)
		Off:	10.0 (3.6)	9.7 (5.0)
Cerebellars	18		16.7 (11.9)	12.3 (4.3)
Corticals	4		12.2 (6.3)	16.2 (6.2)

Table 4

Perception tasks, duration and frequency judgements. Scores are in terms of step differences between lower and upper thresholds. Standard deviations are given in parenthesis.

Group	N	Duration	Frequency
Controls			
College Aged	24	9.8 (6.1)	12.3 (11.0)
Temporal Epilepsy			
Left Focus	16	10.5 (6.0)	17.7 (12.7)
Right Focus	13	9.3 (4.7)	18.8 (12.3)

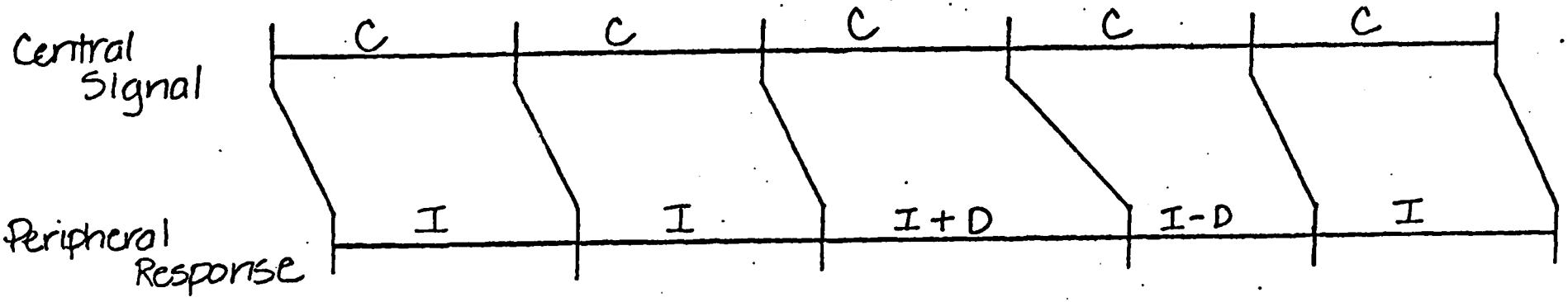
MOTOR PROGRAM -- THROWING A BASEBALL

SUBROUTINES:

SELECT	RIGHT VERSUS LEFT ARM
SEQUENCE	KICK, WINDUP, RELEASE, FOLLOW THROUGH
FORCE	FASTBALL=LARGE; CHANGEUP=SMALL;
TIMING	SNAP WRIST AT RELEASE FOR CURVEBALL

Figure 1: Possible subroutines of the motor program are listed on the left. On the right side are listed hypothesized computations required for each subroutine in order to pitch a baseball.

a. Perfect Clock Process with Peripheral Variability



b. Perfect Implementation Process with Central Variability

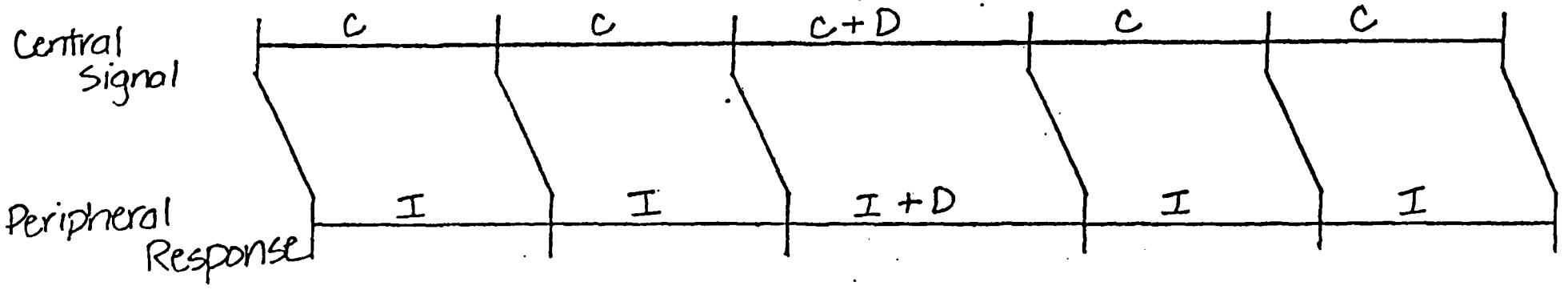


Figure 2: Hypothetical series of inter-response intervals to demonstrate that only peripheral variability produces negative covariation between successive intervals.

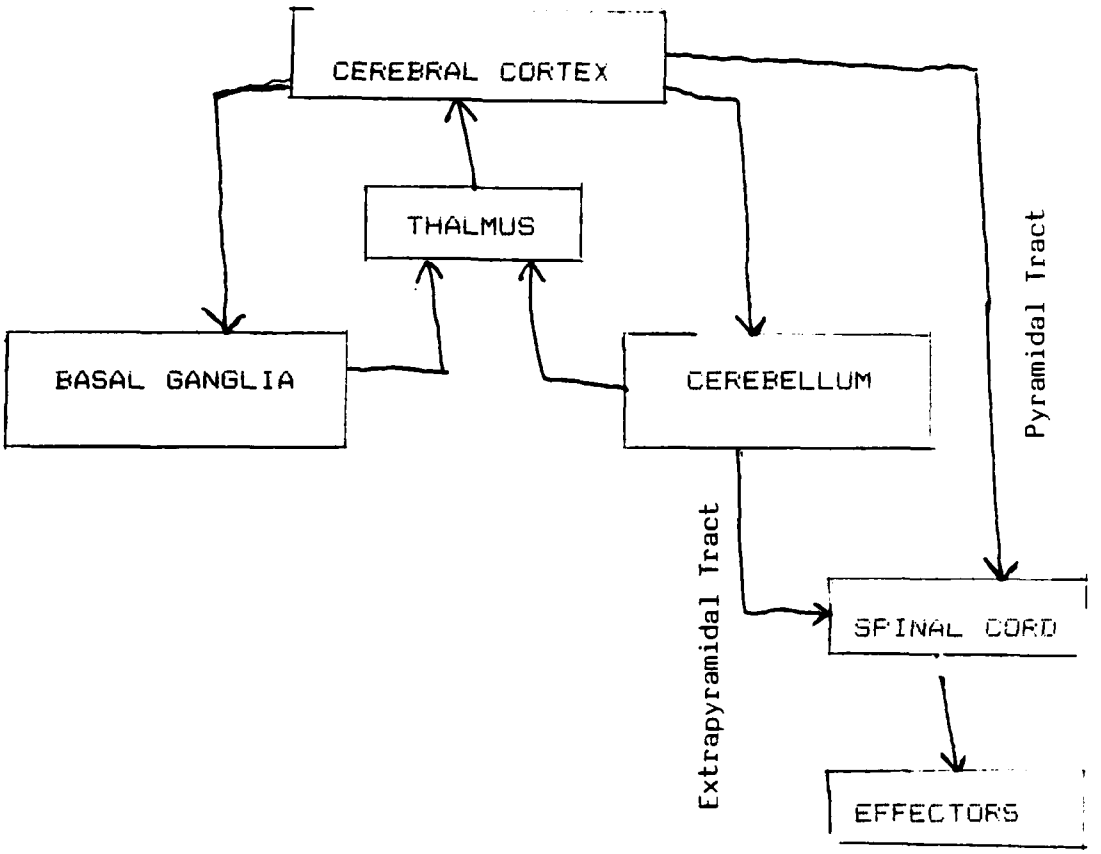


Figure 3: Simplified wiring diagram of the neural structures examined in this study. Variability in the loops which return to the cerebral cortex is hypothesized to constitue timing variance. Motor delay variance is the result of variability in the descending pathways to the spinal cord.

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